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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 08/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/829,504	EPSTEIN ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-46 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-46 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 22-24, 26-28, 30-32, 34-36, 38-40, and 42-46 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See MPEP § 608.01(n). These claims all depend from claims 13 and 14, which are themselves multiple dependent claims. Accordingly, the claims 22-24, 26-28, 30-32, 34-36, 38-40, and 42-46 have not been further treated on the merits.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

1. Claims 1, 2 and 13-16, drawn to an aptamer that binds to PDGF and comprises a sequence selected from SEQ ID NO:1-3, 9-38, 50, 54-90 and 94-99, classified in class 536, subclass 23.1.
2. Claims 3-12 and 13-16, drawn to an aptamer comprising a first sequence capable of binding to a first target, and a second sequence capable of binding to a second target, classified in class 536, subclass 23.1.
3. Claims 17-20, drawn to a composition comprising an aptamer that binds to VEGF, a pharmaceutically acceptable carrier, and an aptamer that binds to PDGF and comprises a sequence selected from SEQ ID NO:1-3, 9-38, 50, 54-90 and 94-99, classified in class 536, subclass 23.1.
4. Claim 29, drawn to a method of reducing interstitial fluid pressure in a tumor comprising the step of administering an aptamer that binds to PDGF

and comprises a sequence selected from SEQ ID NO:1-3, 9-38, 50, 54-90 and 94-99, classified in class 514, subclass 44.

5. Claim 29, drawn to a method of reducing interstitial fluid pressure in a tumor comprising the step of administering an aptamer comprising a first sequence capable of binding to a first target, and a second sequence capable of binding to a second target, classified in class 514, subclass 44.

6. Claim 33, drawn to methods of increasing the permeability of a solid tumor to cytotoxic agents comprising the step of administering an aptamer that binds to PDGF and comprises a sequence selected from SEQ ID NO:1-3, 9-38, 50, 54-90 and 94-99, classified in class 514, subclass 44.

7. Claim 33, drawn to methods of increasing the permeability of a solid tumor to cytotoxic agents comprising the step of administering an aptamer comprising a first sequence capable of binding to a first target, and a second sequence capable of binding to a second target, classified in class 514, subclass 44.

8. Claim 37, drawn to methods of reducing constitutive expression of platelet derived growth factor in a tumor comprising the step of administering an aptamer that binds to PDGF and comprises a sequence selected from SEQ ID NO:1-3, 9-38, 50, 54-90 and 94-99, classified in class 514, subclass 44.

9. Claim 37, drawn to methods of reducing constitutive expression of platelet derived growth factor in a tumor comprising the step of administering an

aptamer comprising a first sequence capable of binding to a first target, and a second sequence capable of binding to a second target, classified in class 514, subclass 44.

10. Claim 41, drawn to methods of reducing angiogenesis and neovascularization in a solid tumor comprising the step of administering an aptamer that binds to PDGF and comprises a sequence selected from SEQ ID NO:1-3, 9-38, 50, 54-90 and 94-99, classified in class 514, subclass 44.

11. Claim 41, drawn to methods of reducing angiogenesis and neovascularization in a solid tumor comprising the step of administering an aptamer comprising a first sequence capable of binding to a first target, and a second sequence capable of binding to a second target, classified in class 514, subclass 44.

Claims 13-16, 29, 33, 37, and 41 are generic to a plurality of patentably distinct inventions listed above. These claims will be examined only to the extent that they are defined by the elected invention.

Claims 21 and 25 link inventions 4, 6, 8, and 10 to the extent that claims 21 and 25 are drawn to methods of treating cancer or a tumor comprising administering an aptamer that binds to PDGF and comprises a sequence selected from SEQ ID NO:1-3, 9-38, 50, 54-90 and 94-99.

Claims 21 and 25 also link inventions 5, 7, 9, and 11 to the extent that claims 21 and 25 are drawn to methods of treating cancer or a tumor comprising administering an

aptamer comprising a first sequence capable of binding to a first target, and a second sequence capable of binding to a second target.

The restriction requirement among linked inventions is subject to the nonallowance of the linking claim(s). Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Should Applicant elect one of groups embracing SEQ ID NOS: 1-3, 9-38, 50, 54-90 and 94-99, then a further election of a single SEQ D NO: will be required. See MPEP 803.02 - PRACTICE RE MARKUSH-TYPE CLAIMS - If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Since the

decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1)share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

Several instant claims are directed SEQ ID NOS: 1-3, 9-38, 50, 54-90 and 94-99 which are aptamers that bind to PDGF. Although the sequences claimed each bind PDGF, the sequences are considered to be unrelated, since each sequence claimed is structurally independent. As such the Markush/genus of sequences in the instant claims is not considered to constitute a proper genus, and is therefore subject to restriction. Furthermore, a search of more than one (1) of the sequences claimed presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed sequences. In view of the foregoing, one (1) sequence is considered to be a reasonable number of sequences for examination if a group drawn to the Markush group is elected. Note that this is not a species election.

The inventions are distinct, each from the other because of the following reasons:

Inventions 1 and 2 are related as subcombination and combination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does

not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because it need not bind PDGF. Also the subcombination need not bind a second target, while the combination must bind two targets. The subcombination has separate utility such as such as treatment of tumors in vivo, whereas the combination can be used to inhibit PDGF activity for any purpose in vitro or in vivo. A similar relationship exists between inventions 2 and 3, between inventions 3, and 4, between inventions 4, and 5, and between inventions 5, and 6.

Inventions 1 and 3 are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because it need not contain an aptamer that binds VEGF. The subcombination has separate utility i.e. the simultaneous inhibition of VEGF and PDGF.

As a result, groups 1-3 are patentably distinct. Accordingly, methods of using the aptamers or compositions according to groups 1-3 are also patentably distinct from each other because they require different reagents, i.e. different aptamers or compositions. Thus groups 4, 6, 8, and 10 are distinct from groups 5, 7, 9, and 11.

Methods according to groups 4, 6, 8, and 10, or groups 5, 7, 9, and 11, which utilize the same aptamer or composition, are distinct for the following reasons. Groups 4 and 5 are directed to methods of reducing interstitial fluid pressure in a tumor. Groups 6 and 7 are directed to methods of increasing the permeability of a solid tumor to cytotoxic agents. Groups 8 and 9 are drawn to methods of reducing constitutive expression of platelet derived growth factor in a tumor. Groups 10 and 11 are drawn to methods of reducing angiogenesis and neovascularization in a solid tumor. While the method steps are the same for inventions requiring administration of the same aptamer or composition, the results of the methods differ. As a result a detailed analysis of the enablement of each method is required. Such an analysis represents an undue burden on the Examiner because the searches are non-coextensive. As a result methods of reducing interstitial fluid pressure in a solid tumor, increasing permeability in a solid tumor, reducing constitutive expression of platelet derived growth factor in a tumor, and reducing angiogenesis and neovascularization in a solid tumor are independent and distinct.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and their recognized divergent subject matter, and because each invention requires a separate, non-coextensive search, restriction for examination purposes as indicated is proper.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See

"Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Peter Paras, can be reached at (571) 272-4517. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Richard Schnizer, Ph.D.
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Art Unit 1635